REMARKS

Claims 1-47 were pending in the instant application. New claims 48-50 have been added. Accordingly, claims 1-50 will be pending in the application upon entry of the new claims presented herein.

Support for the new claims can be found in the specification and the claims as originally filed. Specifically, support for claim 48 can be found in the specification at page 3, lines 32-34; support for claim 49 can be found at page 5, lines 32-38; and support for claim 50 can be found at page 5, lines 32-38. No new matter has been added.

Cancellation of and/or amendments to the claims as originally filed should in no way be construed as an acquiescence to any of the rejections/objections set forth in the instant Office Action, and were made solely to expedite prosecution of the above-identified application. For the convenience of the Examiner, the claims that will be pending upon entry of the instant amendments are attached hereto as Appendix A.

Requirement for Election

The Office Action, on page 2, requires restriction to a single disclosed species, selecting a single example from each of groups I-IV under 35 U.S.C. §121 as follows:

Group I: specific cell type, *e.g.*, yeast or mammalian;

Group II: specific receptor protein, *e.g.*, β_2-adrenergic receptor or STE2;

Group III: specific biochemical pathway, *e.g.*, a particular MAPK pathway, *e.g.*, yeast pheromone response pathway; and

Group IV: specific heterologous DNA construct that encodes a polypeptide that activates a signal transduction pathway;

Applicants are required to elect a single example from each of the above groups for prosecution on the merits.

Accordingly, Applicants hereby elect, with traverse, a yeast cell for Group I; a Ste2 receptor for Group II; a yeast pheromone response pathway for Group III; and Ste5 for Group IV. Claims 2, 7-9, 14-16, 23-27, 29-36, and 38-50 are readable upon Group I; claim 48 is readable upon Group II; claims 7-9, 14-16, 23-27, 29-36, 38-43, and 46-50 are readable upon group III; and claims 9, 15, 16, 32-36, 38- 40, 46, and 47 are readable upon group IV.

The Office Action, on page 3, requires restriction to a single disclosed species, selecting a single example from Species A, and a single example from Species B, under 35 U.S.C. §121 as follows:

> Species type A: each species comprising a specific signal to be amplified, including particular reporter gene constructs.
> Species type B: each species comprising a specific mutation in a particular gene/protein participating in the signal transduction pathway.

Applicants are required to elect a single example from each of the above species for prosecution on the merits. Accordingly, Applicants hereby elect, with traverse, FUS1 as the pheromone-responsive promoter and lacZ as the reporter gene to be amplified for Species A; and a mutated STE5 gene encoding a Ste5 protein having a T52M mutation for Species B. Claims 23, 24, 31-36, 38-40, 46, 47, 49, and 50 are readable upon Species A; and claim 16 is readable upon Species B.

Applicants respectfully traverse the requirement for election, and submit that the requirement is improper.

First, Applicants submit that the subject matter of the various groups represent different embodiments of a single inventive concept for which a single patent should issue. The pending claims represent an intricate web of knowledge, continuity of effort, and consequences of a single invention, which merit examination of all embodiments of the invention in a single application. Therefore, it is improper to require that specific embodiments of the invention be prosecuted in separate patent applications.

Additionally, Applicants submit that a sufficient search and examination with respect to the subject matter of all claims can be made without serious burden. As the M.P.E.P. states:

> If the search and examination of an entire application can be made without serious burden, the examiner must examine it on the merits, even though it includes claims to independent or distinct inventions.
>
> M.P.E.P. § 803 (7th ed., Rel. 78A, March 1999).

That is, even if the above-enumerated embodiments of the invention are patentably distinct, the Examiner must still examine the entire application on the merits because doing so will not result in a serious burden.

Applicants submit that a search and examination of all embodiments from each of the six groups (Groups I-IV, A, and B) will have substantial overlap, and no serious burden will result from searching and examining all three groups in the same application. Indeed, the fields of search will be coextensive. This is especially true in light of the fact that the Examiner has not indicated any divergent search classes/subclasses for the various embodiments of the invention. Moreover, to carve up the claims in accordance with the scheme set forth in the instant Office Action will require Applicants to file and prosecute numerous patent applications at substantial cost. Therefore, Applicants propose that all species/embodiments encompassed by the claims as filed be searched and examined in the instant application.

CONCLUSION

In view of the foregoing arguments in traversal, and in the interests of efficiency and cost savings, Applicants respectfully request reconsideration and withdrawal of the requirement for species election. Applicants also state their understanding that even if the requirement is made final, the claims will not be limited to the foregoing elected species unless a generic claim is not found to be allowable. If a telephone conversation with Applicants' attorney would help expedite the prosecution of the above-identified application, the Examiner is urged to call Applicants' attorney at (617) 227-7400.

Respectfully submitted,

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Appendix A

What is claimed is:

1. A recombinant cell comprising:
(i) a receptor that, upon ligand stimulation, activates an endogenous signal transduction pathway; and
(ii) a heterologous DNA construct comprising a gene encoding a protein that activates the signal transduction pathway, which gene is operatively linked to a promoter that is responsive to activation of the signal transduction pathway;
wherein stimulation of the receptor by a ligand leads to expression of the heterologous DNA construct encoding the protein that activates the signal transduction pathway such that signals generated by ligand binding to the receptor are amplified.

2. The cell of claim 1, which is a yeast cell.

3. The cell of claim 1, which is a mammalian cell.

4. The cell of claim 1, wherein the receptor is a G protein coupled receptor.

5. The cell of claim 4, wherein the G protein coupled receptor is a heterologous G protein coupled receptor.

6. The cell of claim 1, wherein the endogenous signal transduction pathway is a mitogen activated protein kinase (MAPK) pathway.

7. The cell of claim 2, wherein the endogenous signal transduction pathway is a yeast pheromone response pathway.

8. A recombinant yeast cell comprising :
(i) a heterologous G protein coupled receptor that, upon ligand stimulation, activates an endogenous yeast pheromone response pathway; and
(ii) a heterologous DNA construct comprising a gene encoding a protein that activates the yeast pheromone response pathway, which gene is operatively linked to a promoter that is responsive to activation of the yeast pheromone response pathway

wherein stimulation of the receptor by a ligand leads to expression of the heterologous DNA construct encoding the protein that activates the yeast pheromone response pathway such that signals generated by ligand binding to the receptor are amplified.

9. The yeast cell of claim 8, wherein the gene encoding a protein that activates the yeast pheromone response pathway is STE5.

10. The yeast cell of claim 8, wherein the gene encoding a protein that activates the yeast pheromone response pathway is STE4.

11. The yeast cell of claim 8, wherein the gene encoding a protein that activates the yeast pheromone response pathway is STE12.

12. The yeast cell of claim 8, wherein the gene encoding a protein that activates the yeast pheromone response pathway is STE11.

13. The yeast cell of claim 8, wherein the gene encoding a protein that activates the yeast pheromone response pathway is a dominant truncation allele of STE20.

14. The yeast cell of claim 8, wherein the gene encodes a hypersensitive mutant form of the protein that activates the yeast pheromone response pathway.

15. The yeast cell of claim 14, wherein the hypersensitive mutant form is a mutant Ste5 protein.

16. The yeast cell of claim 15, wherein the mutant Ste5 protein has a T52M mutation or T52M,S18R mutations.

17. The yeast cell of claim 14, wherein the hypersensitive mutant form is a mutant Ste4 protein.

18. The yeast cell of claim 17, wherein the mutant Ste4 protein has a mutation selected from the group consisting of G124D; W136G; W136R; ΔL138; W136R,L138F; and W136G,S151C.

19. The yeast cell of claim 14, wherein the hypersensitive mutant form is a mutant Ste11 protein.

20. The yeast cell of claim 19, wherein the mutant Ste11 protein has a T596I mutation (allele Ste11-4) or a P278S mutation (allele Ste11-1).

21. The yeast cell of claim 14, wherein the hypersensitive mutant form is a mutant Fus3 protein.

22. The yeast cell of claim 21, wherein the mutant Fus3 protein has a I161L mutation.

23. The yeast cell of claim 8, wherein the promoter that is responsive to activation of the yeast pheromone response pathway is selected from the group consisting of: FUS1, AGA1, FAR1, and FUS2.

24. The yeast cell of claim 23, wherein the promoter is a FUS1 promoter.

25. The yeast cell of claim 8, wherein an endogenous yeast gene encoding a protein that negatively regulates the yeast pheromone system pathway is mutated to render the protein nonfunctional.

26. The yeast cell of claim 25, wherein the endogenous gene that is mutated encodes a phosphatase that negatively regulates the yeast pheromone system pathway.

27. The yeast cell of claim 26, wherein the endogenous gene encoding the phosphatase is selected from the group consisting of: MSG5, PTP2, and PTP3.

28. The yeast cell of claim 8, which further comprises a reporter gene construct that produces a detectable signal upon activation of the yeast pheromone response pathway.

29. The yeast cell of claim 8, wherein the heterologous DNA construct is carried by a high copy number plasmid.

30. The yeast cell of claim 8, wherein the heterologous DNA construct is carried by a low copy number plasmid.

31. The yeast cell of claim 8, which is a *Saccharomyces cerevisiae* cell.

32. A recombinant yeast cell comprising :
(i) a heterologous G protein coupled receptor that, upon ligand stimulation, activates an endogenous yeast pheromone response pathway; and
(ii) a heterologous DNA construct comprising a STE5 or STE4 gene encoding a Ste5 or Ste4 protein, respectively, that activates the yeast pheromone response pathway, which gene is operatively linked to a FUS1 promoter that is responsive to activation of the yeast pheromone response pathway
wherein stimulation of the receptor by a ligand leads to expression of the heterologous DNA construct encoding the Ste5 or Ste4 protein that activates the yeast pheromone response pathway such that signals generated by ligand binding to the receptor are amplified.

33. The yeast cell of claim 32, wherein the gene encodes a hypersensitive mutant form of the Ste5 or Ste4 protein that activates the yeast pheromone response pathway.

34. The yeast cell of claim 32, wherein an endogenous yeast gene encoding a protein that negatively regulates the yeast pheromone system pathway is mutated to render the protein nonfunctional.

35. The yeast cell of claim 34, wherein the endogenous gene that is mutated encodes a phosphatase that negatively regulates the yeast pheromone system pathway.

36. The yeast cell of claim 35, wherein the endogenous gene encoding the phosphatase is selected from the group consisting of: MSG5, PTP2, and PTP3.

37. The yeast cell of claim 32, which further comprises a reporter gene construct that produces a detectable signal upon activation of the yeast pheromone response pathway.

38. The yeast cell of claim 32, wherein the heterologous DNA construct is carried by a high copy number plasmid.

39. The yeast cell of claim 32, wherein the heterologous DNA construct is carried by a low copy number plasmid.

40. The yeast cell of claim 32, which is a *Saccharomyces cerevisiae* cell.

41. A recombinant yeast cell comprising:

a heterologous G protein coupled receptor that, upon ligand stimulation, activates an endogenous yeast pheromone response pathway,

wherein an endogenous yeast gene encoding a protein that negatively regulates the yeast pheromone system pathway is mutated to render the protein nonfunctional such that signals generated by ligand binding to the receptor are amplified.

42. The yeast cell of claim 41, wherein the endogenous gene that is mutated encodes a phosphatase that negatively regulates the yeast pheromone system pathway.

43. The yeast cell of claim 42, wherein the endogenous gene encoding the phosphatase is selected from the group consisting of: MSG5, PTP2, and PTP3.

44. A recombinant yeast cell comprising :

a heterologous G protein coupled receptor that, upon ligand stimulation, activates an endogenous yeast pheromone response pathway,

wherein an endogenous FUS3 gene is mutated to encode a supersensitive form of Fus3 protein such that signals generated by ligand binding to the receptor are amplified.

45. The yeast cell of claim 44, wherein the supersensitive form of Fus3 protein has a I161L mutation.

46. An assay to identify compounds that modulate the activity of a receptor, comprising:

(i) providing a recombinant cell as claimed in claim 1, 8, 32, 41 or 44, wherein a detectable signal is produced in the cell upon stimulation of the receptor;

(ii) contacting the cell with a test compound; and

(iii) identifying a compound which induces a change in the detectable signal in the cell, such a change indicating that the compound modulates the activity of the receptor.

47. The assay of claim 46, wherein the cell comprises a reporter gene construct that produces a detectable signal upon receptor stimulation.

48. (New) The yeast cell of claim 8, wherein the G protein coupled receptor is STE2.

49. (New) The yeast cell of claim 28, wherein the reporter gene is lacZ.

50. (New) The yeast cell of claim 28, wherein the reporter gene construct that produces a detectable signal is a FUS-1 promoter operatively linked to lacZ.